

**74I-0794-000972**

**PHARMAKON RESEARCH INTERNATIONAL, INC.**  
WAVERLY, PENNSYLVANIA 18471



84940000072

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FYI-94-000972  
INIT 07/26/94

Acute Oral Toxicity Study  
in Rats (14 Day) 83 EPA/OECD

PH 402-ET-010-84

Saytex 115

Lot# 5315-61

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1984

Submitted to

Ethyl Corporation  
Baton Rouge, Louisiana

Victor T. Mallory, B.S.  
Victor T. Mallory, B.S.  
Study Director

Date

November 16, 1984

Robert W. Naismith  
Robert W. Naismith, Ph.D.

Date

November 16, 1984

Richard J. Matthews  
Richard J. Matthews, Ph.D.  
President

Date

November 14, 1984

Acute Oral Toxicity Study in Rats  
14 Day  
83 EPA/OECD

PH 402-ET-010-84

SUMMARY

In a dose-range finding, six groups of four rats (two male and two female) were orally administered Saytex 115, Lot# 5315-61, at 500, 2500, 5000 (as received), 5000 (vehicle), 7500 and 10,000 mg/kg. Signs observed included wet pelage, diarrhea, piloerection, abnormal gait, abnormal stance, hunched body position, tremors, pre-convulsive behavior, chromodacryorrhea, nasal discharge (red) and loss of righting reflex. None of the animals died at the 500, 2500 or the 5000 (as received) mg/kg dose levels. One of four animals died at the 5000 (vehicle) and 7500 mg/kg dose levels. Two of four rats died at 10,000 mg/kg dose level.

Test article, Saytex 115, Lot# 5315-61, was orally administered to one group of ten animals at a single dose of 5000 mg/kg (as received). Signs observed were decreased activity, diarrhea, piloerection, decreased muscle tone, abnormal gait, abnormal stance, body drop, tremors, prostration, slow righting reflex, and brown discoloration of the nasal region. Five of the ten animals died during the study. Necropsy of the animals dying on study revealed fluid-filled intestines, dark patchy areas on the lungs, dark red adrenals, multiple lesions on the stomach mucosa and a pale liver. Terminal necropsy revealed no test article related lesions.

Based upon the results from the Acute Oral Toxicity Study in Rats, the estimated acute oral LD<sub>50</sub> for Saytex 115, Lot# 5315-61 was determined to be 5000 mg/kg.

Acute Oral Toxicity Study in Rats (14 Day)  
83 EPA/OECD

PH 402-ET-010-84

Sponsor: Ethyl Corporation  
8000 GSRI Avenue  
Baton Rouge, Louisiana 70820

Testing Facility: Pharmakon Research International, Inc.  
Waverly, Pennsylvania 18471

Test Facility  
S.O.P. No.: PH-402

Study No.: PH 402-ET-010-84

Purpose of the Study: To determine the acute single dose oral toxicity of the test material.

Ownership of the Study: The sponsor owns the study. All raw data, analysis, and reports are the property of the sponsor.

Study Monitor: Mrs. Beverly Pancamo, Ethyl Corporation

Study Director: Victor T. Mallory, B.S., Pharmakon Research International, Inc.

Technical Performance: Victor T. Mallory, B.S., Susan E. Armondi and Gary G. Bolus, B.A.

Q.A.U. Responsible Personnel: Leslie Maas, B.S.

Dates of Performance: October 18, 1984 through November 1, 1984

Good Laboratory Practices Statement: This study was conducted in compliance with the Good Laboratory Practice Regulations except if noted.

There were no significant deviations from the GLP Regulations which affected the quality or integrity of the study. Q.A.U. findings derived from the inspection(s) during the conduct of this study and

Acute Oral Toxicity Study in Rats 83 EPA/OECD  
14 Day  
PH 402-ET-010-84

from the audit of the final report are documented and have been provided to the study director and the test facility management.

Record Maintained:

All raw data, final reports, documentation and protocol will be maintained in the central files of Pharmakon Research International, Inc.

Recording:

Standard Pharmakon Notebook

Notebook Reference:

Notebook# 402, pages 76-77, 79-80

Notebook# 1019, pages 107-119

Raw Data:

Copies of notebook and necropsy recordings attached.

Statistics:

Not applicable

TEST ARTICLE

Compound Description:

Saytex 115 -- amber semi-solid

Lot No.:

5315-61

Base Factor:

Not applicable

Amount Submitted:

800 grams

Date Submitted:

September 28, 1984

Special Handling Instructions:

Standard precautions

Analysis of Purity:

The purity, identity, strength and stability of the test article are the responsibility of the sponsor.

Stability:

There was no apparent change in the physical state of the test article during administration.

TEST SYSTEM

Species:

Rat

Strain:

Sprague Dawley

Supplier (Source): Charles River Breeding Laboratory, Wilmington, Massachusetts

Sex: Male and female

Age at Initiation: Young adult animals were used. The weight variation of animals used in the test did not exceed  $\pm$  20% of the mean weight for each sex.

No. on Study: Dose-range finding study -- twenty four (24)  
Single dose level -- ten (10)

Method and Justification for Randomization: Selection based upon body weight

Acclimation Period: Five (5) days

System of Identification: Cages marked with an animal number and dose level.  
Rats were identified by metal numbered ear tag.

**HUSBANDRY**

Research Facility Registration: U.S.D.A. Registration No. 23-107 under the Animal Welfare Act 74: SC 2131 et seq.

Animal Rooms: Separate isolation by test system.  
Light cycle - 12 hours light, 12 hours dark.  
Temperature/Humidity - maintained at a temperature of 22°C  $\pm$  3°C, and a humidity of 30 to 70%.

Housing: Rats housed individually in stainless steel  $\frac{1}{4}$ " wire mesh cages. Size in accordance with the "Guide for the Care and Use of Laboratory Animals" of the Institute of Laboratory Resources, National Research Council.

Sanitization: Waste material removed daily. Cages and feeders were sanitized every two weeks.

Acute Oral Toxicity Study in Rats 83 EPA/OECD  
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Food: Wayne Lab Blox<sup>R</sup>, ad libitum, checked daily and added or replaced as needed. Feeders were designed to reduce soiling, bridging and scattering.

Food Analysis: There were no contaminants that were reasonably expected to be present in the dietary material known to be capable of interfering with the purpose or conduct of the study.

Water Analysis: Availability - fresh tap water, ad libitum. Water is monitored for contaminants at periodic intervals according to Standard Operating Procedure PH-018.

#### METHODS

Rationale for Test System: According to the New and Revised Health Effect Test Guidelines EPA 560/6-83-001.

Compound Preparation: Test article dosed as received

Dose Administration: 5000 mg/kg

Rationale for Dose Selection: Based on the results of a dose-range finding study.

Volume Administration: 5.0 ml/kg

Vehicle: As received

Route of Administration: Oral, by gavage

Rationale for Route of Administration: According to the New and Revised Health Effect Test Guidelines EPA 560/6-83-001.

Acute Oral Toxicity Study in Rats 83 EPA/OECD  
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Frequency and Duration of Administration: Once (1)

No. of Animals Per Dose Group: Dose-range finding study -- Four (4) (two males and two females)  
Single dose level -- Ten (10) (five males and five females)

No. and Code of Dose Group: Rat No. 5189-5198 Dose Level 5000 mg/kg

Length of Study: Fourteen (14) days

Method of Study Performance: Dose-Range Finding Study  
In a dose-range finding, six groups of four rats (two male and two female) were orally administered Saytex 115, Lot# 5315-61, at 500, 2500, 5000 (as received), 5000 (vehicle), 7500 and 10,000 mg/kg. Signs observed included wet pelage, diarrhea, piloerection, abnormal gait, abnormal stance, hunched body position, tremors, pre-convulsive behavior, chromodacryorrhea, nasal discharge (red) and loss of righting reflex. None of the animals died at the 500, 2500 or the 5000 (as received) mg/kg dose levels. One of four animals died at the 5000 (vehicle) and 7500 mg/kg dose levels. Two of four rats died at 10,000 mg/kg dose level.

Limit Test  
In the limit test, one group of ten rats (5 males and 5 females) was fasted for eighteen hours and orally administered the test article at 5000 mg/kg. The rats were observed immediately after dosing and at one, two, four and twenty-four hours, twice daily through Day 4 and daily thereafter for pharmacotoxic, CNS

effects and mortality. Exact times for each observation period were recorded. On Days -1, 0, 1, 4, 7, 14 and at death, body weights were recorded. The rats were sacrificed by CO<sub>2</sub> inhalation and a gross necropsy performed.

Results:

Signs observed were decreased activity, diarrhea, piloerection, decreased muscle tone, abnormal gait, abnormal stance, body drop, tremors, prostration, slow righting reflex and brown discoloration of the nasal region. Five of the ten animals died during the study. Necropsy of the animals dying on study revealed fluid-filled intestines, dark patchy areas on the lungs, dark red adrenals, multiple lesions on the stomach mucosa and a pale liver. Terminal necropsy revealed no test article related lesions.

Conclusion:

Based upon the results from the Acute Oral Toxicity Study in Rats, the estimated acute oral LD<sub>50</sub> for Saytex 115, Lot# 5315-61 was determined to be 5000 mg/kg.

Table 1  
 Individual and Group Mean Body Weights (grams)  
 Acute Oral Toxicity Study in Rats (14 Day)

PH 402-ET-010-84  
 Saytex 115  
 Lot #5315-61

Males

| Animal No. | Sex | Day -1 | Initial | Day 1    | Day 4   | Day 7   | Final   |
|------------|-----|--------|---------|----------|---------|---------|---------|
| 5189       | M   | 287    | 265     | 283      | 290     | 316     | 364     |
| 5190       | M   | 270    | 246     | 259      | 296     | 305     | 333     |
| 5191       | M   | 262    | 238     | 250      | 218     | d       | d       |
| 5192       | M   | 268    | 243     | 244      | 236     | 260     | 311     |
| 5193       | M   | 278    | 255     | 266      | 248     | 200     | d       |
| $\bar{x}$  |     | 273.00 | 249.40  | 216.40   | 257.60  | 270.25  | 336.00  |
| (S.D.)     |     | (9.70) | (10.69) | (108.23) | (34.10) | (52.73) | (26.63) |

Females

| Animal No. | Sex | Day -1 | Initial | Day 1  | Day 4   | Day 7   | Final  |
|------------|-----|--------|---------|--------|---------|---------|--------|
| 5194       | F   | 187    | 168     | 173    | 158     | 192     | 215    |
| 5195       | F   | 201    | 184     | 193    | 159     | d       | d      |
| 5196       | F   | 187    | 169     | 179    | 160     | 122     | d      |
| 5197       | F   | 200    | 175     | 188    | 190     | 201     | 226    |
| 5198       | F   | 185    | 169     | 170    | 146     | d       | d      |
| $\bar{x}$  |     | 192.00 | 173.00  | 180.60 | 162.60  | 171.67  | 220.50 |
| (S.D.)     |     | (7.81) | (6.75)  | (9.76) | (16.33) | (43.25) | (7.78) |

d - Denotes animals dying on study.

**Table 2**  
**Onset and Duration of Signs at 5000 mg/kg**

**Acute Oral Toxicity Study in Rats (14 Day)**  
 PH 402-ET-010-84  
 Saytex 115  
 Lot #5315-61

**Males**

| <b>Time of Observation</b> | <b>Signs Observed</b>   |
|----------------------------|---|
| Immediate                  | No signs  |
| 1 hour                     | No signs  |
| 2 hour - 24 hours          | Decreased activity  |
| Day 2-5                    | No signs  |
| Day 6                      | Piloerection  |
| Day 7                      | Decreased activity  |
| Day 8                      | Brown discoloration nasal-oral region,<br>piloerection, prostration, tremors. |
| Day 9-14                   | No signs  |

**Females**

|                |  |
|----------------|--|
| Immediate      | No signs   |
| 1 hour         | No signs   |
| 2 hour         | Decreased activity   |
| 4 hour - Day 4 | No signs   |
| Day 5          | Diarrhea, brown discoloration<br>nasal-oral region.  |
| Day 6          | Decreased activity, diarrhea, piloerection,<br>decreased body tone, abnormal stance,<br>abnormal gait.   |
| Day 7          | Decreased activity, decreased body<br>tone, abnormal stance, abnormal gait,<br>brown discoloration nasal-oral region,<br>tremors.                            |
| Day 8          | Piloerection, decreased body tone,<br>abnormal stance, abnormal gait, body<br>drop, brown discoloration nasal-oral<br>region, tremors, slow righting reflex. |
| Day 9-14       | No signs   |

Table 3

## Summary of Mortality

## Acute Oral Toxicity Study in Rats (14 Day)

PH 402-ET-010-84

Saytex 115  
Lot #5315-61

| Dose         | Sex | No. of Rats | Dose Range Study |   |   |   |   |   |   |   |   |    |    |    | Total Mortality |     |
|--------------|-----|-------------|------------------|---|---|---|---|---|---|---|---|----|----|----|-----------------|-----|
|              |     |             | 1                | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13              |     |
| 500 mg/kg    | M   | 2           | 0                | 0 | - | - | - | - | - | - | - | -  | -  | -  | -               | 0/2 |
| 500 mg/kg    | F   | 2           | 0                | 0 | - | - | - | - | - | - | - | -  | -  | -  | -               | 0/2 |
| 2500 mg/kg   | M   | 2           | 0                | 0 | - | - | - | - | - | - | - | -  | -  | -  | -               | 0/2 |
| 2500 mg/kg   | F   | 2           | 0                | 0 | - | - | - | - | - | - | - | -  | -  | -  | -               | 0/2 |
| 5000 mg/kg   | M   | 2           | 0                | 0 | - | - | - | - | - | - | - | -  | -  | -  | -               | 0/2 |
| 5000 mg/kg   | F   | 2           | 0                | 0 | - | - | - | - | - | - | - | -  | -  | -  | -               | 0/2 |
| 5000 mg/kg   | M   | 2           | 0                | 0 | - | - | - | - | - | - | - | -  | -  | -  | -               | 1/2 |
| 5000 mg/kg   | F   | 2           | 0                | 0 | - | - | - | - | - | - | - | -  | -  | -  | -               | 1/2 |
| 7500 mg/kg   | M   | 2           | 0                | 0 | - | - | - | - | - | - | - | -  | -  | -  | -               | 0/2 |
| 7500 mg/kg   | F   | 2           | 0                | 1 | - | - | - | - | - | - | - | -  | -  | -  | -               | 1/2 |
| 10,000 mg/kg | M   | 2           | 0                | 0 | - | - | - | - | - | - | - | -  | -  | -  | -               | 1/2 |
| 10,000 mg/kg | F   | 2           | 0                | 1 | - | - | - | - | - | - | - | -  | -  | -  | -               | 1/2 |
| Limit Test   |     |             |                  |   |   |   |   |   |   |   |   |    |    |    |                 |     |
| 50000 mg/kg  | M   | 5           | 0                | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0  | 0  | 0  | 0               | 2/5 |
| 50000 mg/kg  | F   | 5           | 0                | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 0  | 0  | 0  | 0               | 3/5 |

Table 4

Necropsy Observations  
(Incidence Values)

Acute Oral Toxicity Study in Rats (14 Day)

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Saytex 115  
Lot #5315-61

| Observations                                    | Incidence |   | Terminal Necropsy |   |
|---|-----------|---|-------------------|---|
|   | M         | F | M                 | F |
| <u>Lung</u><br>dark patchy areas                | 1         | - | *                 | * |
| <u>Liver</u><br>pale                            | -         | 1 |                   |   |
| <u>Adrenals</u><br>dark red                     | 1         | - |                   |   |
| <u>Intestines</u><br>fluid-filled<br>discolored | 2         | 3 |                   |   |
| 2   | 3         |   |                   |   |
| <u>Stomach</u><br>Multiple lesions              | 1         | 1 |                   |   |

\*No test article related lesions were observed at terminal necropsy.

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QUALITY ASSURANCE UNIT STATEMENT

This study was conducted in compliance with the Principles of Good Laboratory Practice (GLP) as promulgated by the following regulatory agencies:  
U.S. Food and Drug Administration, as stated in the Code of Federal Regulations, Title 21, Part 58, revised as of April 1, 1980.  
U.S. Environmental Protection Agency as stated in the Federal Register, Vol. 48, No. 230, Tuesday, November 29, 1983.  
Organization for Economic Co-operation and Development Guidelines for Testing Chemicals (OECD), ISBN 92-64-12221-4, adopted by the council at its 535th meeting on 12th May, 1981.

Study No. PH 402-ET-010-84

The following inspections were performed:

| Interval               | Date            |
|------------------------|-----------------|
| <u>In Life Phase</u>   | <u>10/18/84</u> |
| <u>Reporting Phase</u> | <u>11/13/84</u> |
|                        |                 |
|                        |                 |
|                        |                 |

Results of the above inspections were submitted to the Study Director and Management during the course of the study.

11/13/84  
Date

  
Vicki Maas  
Quality Assurance Unit

PHARMAKON RESEARCH INTERNATIONAL, INC.

WAVERLY, PENNSYLVANIA 18471

Compliance Statement

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This study was conducted in compliance with the Principles of Good Laboratory Practice (GLP) as promulgated by the following regulatory agencies:

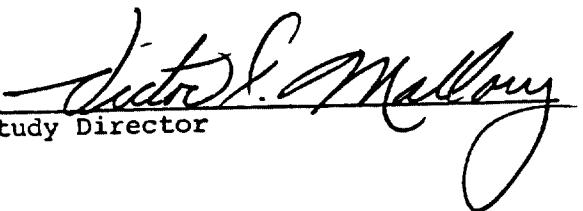
U.S. Food and Drug Administration, as stated in the Code of Federal Regulations, Title 21, Part 58, revised as of April 1, 1980.

U.S. Environmental Protection Agency as stated in the Federal Register, Vol. 48, No. 230, Tuesday, November 29, 1983.

Organization for Economic Co-operation and Development Guidelines for Testing Chemicals (OECD), ISBN 92-64-12221-4, adopted by the council at its 535th meeting on 12th May, 1981.

Study No.: PH 402-FT-010-84

"To the best of my knowledge, the study was conducted in accordance with applicable Good Laboratory Practice regulations; there were no deviations from these regulations that significantly impacted on study conclusions."

  
Study Director

11/16/84  
Date

Study Monitor

                  
Date

E Acute Exposure Oral Toxicity  
dose range

n Page No.

Sponsor: Ethyl Corporation

Purpose: To determine dose levels for the LD<sub>50</sub>.

Species: Rat Strain: Sprague Dawley

Sex: male(♂) and female(♀)

Weight: Weight variations not to exceed  $\pm 20\%$  of mean wt. for each sex

No. on study: twelve (12) 4/litter (3♂) + 12 (4/litter, 3♂) - total as per request

Animal PO#.: 091784 A TOX Food lot #: 8234

Animal Identification: Cages marked with group no. and dose level

Test Article: PBDPO Lot # 5315-61

Description: Amber semi-solid

Amt. submitted: 1095g. (m+c) receipt date: 9/28/84

route: oral, by gavage

Vehicle: Corn oil

Dose levels: 500, 2500, 5000 mg/kg + 5000 (as vehicle), 7500, 10,000 mg/kg.

Light Cycle checked: 9/30/84 SEA

Scale #: 10

Length of Study: 72 hrs.

Date of Initiation: 10/1/84 10/3/84 (additional levels added)

Date of Termination: 10/4/84 10/6/84 (as per sponsor's request)

Compound Preparation: 10/1/84 SEA

@ 500 mg/kg  $\rightarrow$  1000 mg test article q.s. 10ml with corn oil@ 2500 mg/kg  $\rightarrow$  5000 mg test article q.s. 10ml with corn oil@ 5000 mg/kg  $\rightarrow$  as received

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LE Acute Exposure Oral Toxicity  
(Same Dose)

In Page No. 76

| Rat # | Sex | Compound/<br>Dose | Initial<br>wt.<br>(grams) | ml.<br>admin. | Dose<br>time | No. dead | Final<br>wt.<br>(grams) |
|-------|-----|-------------------|---------------------------|---------------|--------------|----------|-------------------------|
| 1     | ♂   | BDPO<br>300mg/kg  | 211                       | 1.1           | 11:56        | 0/4      | 240                     |
| 2     | ♂   | BDPO<br>300mg/kg  | 243                       | 1.2           |              | 0/4      | 294                     |
| 3     | ♀   | BDPO<br>300mg/kg  | 205                       | 1.0           |              | 0/4      | 215                     |
| 4     | ♀   | BDPO<br>300mg/kg  | 231                       | 1.2           | 11:57        | 0/4      | 238                     |
| 5     | ♂   | BDPO<br>300mg/kg  | 210                       | 1.1           | 11:58        | 0/4      | 245                     |
| 6     | ♂   | BDPO<br>300mg/kg  | 228                       | 1.1           |              | 0/4      | 258                     |
| 7     | ♀   | BDPO<br>300mg/kg  | 187                       | 0.9           |              | 0/4      | 176                     |
| 8     | ♀   | BDPO<br>300mg/kg  | 200                       | 1.0           | 12:00        | 0/4      | 209                     |
| 9     | ♂   | BDPO<br>300mg/kg  | 222                       | 0.49          | 12:01        | 0/4      | 248                     |
| 10    | ♂   | BDPO<br>300mg/kg  | 223                       | 0.49          |              | 0/4      | 259                     |
| 11    | ♀   | BDPO<br>300mg/kg  | 212                       | 0.47          |              | 0/4      | 187                     |
| 12    | ♀   | BDPO<br>300mg/kg  | 219                       | 0.48          | 12:23        | 0/4      | 220                     |

10/1/84 SEA 10/1/84 SEA 10/1/84 SEA

10/4/84 GCB

immediate post dose observation: @ 300mg/kg: NO signs  
 @ 2500mg/kg: no signs @ 5000mg/kg: NO Signs 10/1/84 SEA  
 1 hr. post dose observation: @ 500mg/kg: NO signs  
 @ 2500mg/kg: no signs @ 5000mg/kg: NO signs 10/1/84 SEA  
 4 hr. post dose observation: @ 500mg/kg: NO signs  
 @ 2500mg/kg: no signs @ 5000mg/kg: NO signs 10/1/84 SEA  
 24 hr. post dose observation: @ 500mg/kg: NO signs  
 @ 2500mg/kg: ½♂ no signs ½♀ no signs ½♀ wet pelage  
 (yellow) and genital region @ 5000mg/kg: NO signs 10/2/84 GCB  
 48 hr. post dose observation: @ 500mg/kg: NO signs  
 @ 2500mg/kg: no signs @ 5000mg/kg: NO signs 10/3/84 SEA  
 48 hr. 72 h.p.d. @ 500mg/kg: no signs @ 2500mg/kg: ½♂ no signs, ½♀ signs, ½♀ alopecia.  
 @ 5000mg/kg: no signs. 10/4/84 GCB

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## TLE Additional Dose Range (as per sponsor request)

From Page No. 77

| Rat # | SEX | Compound/<br>dose | Initial wt<br>(gm) | ml/<br>admin. | Time of<br>dose | No. dead/<br>date | Final wt<br>(gm) |
|-------|-----|-------------------|--------------------|---------------|-----------------|-------------------|------------------|
| 1     | ♂   | PBDPO             | 243                | 3.7           | 11:35AM         |                   | 198              |
| 2     | ♂   | ② 5000 mg/kg      | 220                | 3.3           |                 |                   | 206              |
| 3     | ♀   | ③ 5000 mg/kg      | 196                | 3.0           |                 | 10/6/84           | 171              |
| 4     | ♀   |                   | 219                | 3.3           |                 |                   | 207              |
| 5     | ♂   | PBDPO             | 242                | 3.6           |                 |                   | 184              |
| 6     | ♂   | ② 7,500 mg/kg     | 247                | 3.7           |                 |                   | 196              |
| 7     | ♀   | ③ 7,500 mg/kg     | 189                | 2.8           |                 | 10/5/84           | 166              |
| 8     | ♀   |                   | 209                | 3.1           |                 |                   | 168              |
| 9     | ♂   | PBDPO             | 247                | 3.7           |                 | 10/6/84           | 218              |
| 10    | ♂   |                   | 229                | 3.4           |                 |                   | 185              |
| 11    | ♀   | ② 10,000 mg/kg    | 206                | 3.1           |                 |                   | 191              |
| 12    | ♀   | ③ 10,000 mg/kg    | 213                | 3.2           | 11:44AM         | 10/5/84           | 195              |

10/3/84 GGB

10/6/84 GGB

Compound prep: 10/3/84 GGB

② 5000 mg/kg → 7,500 mg PBDPO qs. 22.5 ml corn oil

③ 7,500 mg/kg → 11,250 mg PBDPO qs. 22.5 ml corn oil

④ 10,000 mg/kg → 15,000 mg PBDPO qs. 22.5 ml corn oil

Immediate observations -

② 5000 mg/kg : 2/2 ♂ no signs, 2/2 ♀ no signs

③ 7,500 mg/kg : 2/2 ♂ no signs, 2/2 ♀ no signs

④ 10,000 mg/kg : 2/2 ♂ no signs, 2/2 ♀ no signs 10/3/84 G.B.

1 hr. pd. ② 5000 mg/kg : 1/2 ♂ no signs, 1/2 ♂ diarrhea, 1/2 ♀ no signs, 1/2 ♀ diarrhea

③ 7,500 mg/kg : 1/2 ♂ no signs, 1/2 ♂ diarrhea, 2/2 ♀ diarrhea

④ 10,000 mg/kg : 1/2 ♂ no signs, 1/2 ♂ diarrhea, 1/2 ♀ diarrhea, no signs. 10/3/84 G.G.B.

4 hr. pd. ② 5000 mg/kg : 2/2 ♂ diarrhea, 2/2 ♀ diarrhea

③ 7,500 mg/kg : 2/2 ♂ diarrhea, 2/2 ♀ diarrhea

④ 10,000 mg/kg : 1/2 ♂ no signs, 1/2 ♂ diarrhea, 2/2 ♀ no signs

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LE Additional Dose Range (as per sponsor's request)

m Page No. 79

## Observations

24 Hr. p.d. @ 5000 mg/kg:  $\frac{1}{2} \text{♂}$  red discoloration nasal area, pilo-erection, excessive diarrhea, abnormal gait & stance, hunched body position, tremors.

$\frac{1}{2} \text{♀}$  red discoloration nasal area, pilo-erection, excessive diarrhea, abnormal gait & stance, hunched body position, tremors, pre-convulsive behavior.

@ 7,500 mg/kg:  $\frac{1}{2} \text{♂}$ ,  $\frac{1}{2} \text{♀}$  red discoloration nasal area, pilo-erection, excessive diarrhea, abnormal gait & stance, hunched body position, tremors, pre-convulsive behavior, rhinodacryorrhea, ptosis.

@ 10,000 mg/kg:  $\frac{1}{2} \text{♂}$ ,  $\frac{1}{2} \text{♀}$  red discoloration nasal area, pilo-erection, excessive diarrhea, abnormal gait & stance, hunched body position, tremors, pre-convulsive behavior, rhinodacryorrhea, ptosis. 10/4/84 GGB.

48 Hr. p.d. @ 5000 mg/kg:  $\frac{1}{2} \text{♂}$  red discoloration nasal area, pilo-erection, excessive diarrhea, abnormal gait & stance,  $\frac{1}{2} \text{♀}$  red discoloration nasal area, pilo-erection, excessive diarrhea, abnormal gait & stance, tremors, pre-convulsive behavior,  $\frac{1}{2} \text{♀}$  diarrhea, abnormal gait & stance, red discoloration nasal area.

@ 7,500 mg/kg:  $\frac{1}{2} \text{♂}$  pilo-erection, rhinodacryorrhea, diarrhea, tremors,  $\frac{1}{2} \text{♂}$  pre-convulsive behavior,  $\frac{1}{2} \text{♀}$  dead,  $\frac{1}{2} \text{♀}$  tumors, diarrhea, pilo-erection, abnormal gait & stance, pre-convulsive behavior

@ 10,000 mg/kg:  $\frac{1}{2} \text{♂}$  diarrhea, tremors, pre-convulsive behavior, pilo-erection, red discoloration nasal area, abnormal gait & stance,  $\frac{1}{2} \text{♂}$  decreased activity, slow righting, ptosis,  $\frac{1}{2} \text{♀}$  dead,  $\frac{1}{2} \text{♀}$  diarrhea, red discoloration nasal area, pilo-erection, abnormal gait & stance, tremors, pre-convulsive behavior. 10/5/84

72 M p.d. @ 5000 mg/kg:  $\frac{1}{2} \text{♂}$  red discoloration nasal area, pilo-erection,  $\frac{1}{2} \text{♂}$  excessive diarrhea, pre-convulsive behavior, abnormal stance & gait,  $\frac{1}{2} \text{♀}$  dead,  $\frac{1}{2} \text{♀}$  diarrhea, tremors, red discoloration nasal area.

@ 7500 mg/kg:  $\frac{1}{2} \text{♂}$  pilo-erection, rhinodacryorrhea, diarrhea, tremors, pre-convulsive behavior,  $\frac{1}{2} \text{♀}$  diarrhea, pilo-erection, pre-convulsive behavior, tremors.

@ 10,000 mg/kg:  $\frac{1}{2} \text{♂}$  dead,  $\frac{1}{2} \text{♂}$  pilo-erection, red discoloration nasal area, pre-convulsive behavior,  $\frac{1}{2} \text{♀}$  dead. 10/4/84

## ACUTE TOXICOLOGY STUDY ASSIGNMENT FORM

Title: Acute Exposure Oral Toxicity study No. PH402-ET-010-84

Sponsor: Ethyl Corporation

Purpose: To evaluate the single-dose oral toxicity and/or to determine the LD<sub>50</sub> of the test article.

Method: refer to protocol PH402 EPA/OECD (modified)

Date of Initiation: 10/18/84 Date of Termination: 11/1/84

Test Article: Autex 115

and Description: Amber semi-solid

Vehicle: N/A

Dose Levels: 5000mg/kg

Route of Administration: Oral, by gavage

Animal P.O. #: 100/84 FTOX

Species: Rat

Strain: Sprague Dawley

Weight Range: Young, Adult Animals

Food Lot #: 8234, 9044

No. of Animals on Study: Ten (10)

Sex: Male Five (5)

Female Five (5)

Scale #: 10

Light cycle checked: 10/17/84 SEA

Animals shave/fluorescein N/A

pH of Test Article: N/A

Compound Preparation: As received

Dose Level: \_\_\_\_\_ Test Weight: \_\_\_\_\_ Final Volume: \_\_\_\_\_

Comments: \_\_\_\_\_

Investigator: Suzanne Almond Date 11/1/84

Study Director: District Manager Date 11/1/84

## Ethylenimine International

Sponsor Ethylenimine

Test Article 1-PPDI-DE Gluteral 115 mg/ml

Study No. PHY402-ET-010-84

## ACUTE TOXICITY

Species Rat

S.O.P. PHY402 83 (EPAA/ECDO) modified

LD<sub>50</sub>

Vehicle N/A

Route Oral

IP

IV

SC

Room #

TOV. III/I

COMPOUND PREPARATION: As received

AM Observations

ATE: 10/18/84

DOSE: 500mg/kg

VOLUME: 5ml/kg

| ANIMAL # | SEX | INITIAL WT. (gm) | DOSE ADM. (ml) | TIME  | FINAL WT. | DATE OF DEATH |
|----------|-----|------------------|----------------|-------|-----------|---------------|
|          |     |                  |                |       |           |               |
| 5189     | ♂   | 265              | 0.6            | 9:40  | 3164      |               |
|          |     | 290              |                |       |           |               |
| 5190     | ♂   | 246              | 0.5            |       | 333       |               |
|          |     | 296              |                |       |           |               |
| 5191     | ♂   | 238              | 0.5            |       | 177       |               |
|          |     | 218              |                |       |           | 10/24/84      |
| 5192     | ♂   | 243              | 0.5            |       | 311       |               |
|          |     | 236              |                |       |           |               |
| 5193     | ♂   | 255              | 0.6            |       | 187       |               |
|          |     | 248              |                |       |           | 10/27/84      |
| 5194     | ♀   | 168              | 0.4            |       | 215       |               |
|          |     | 158              |                |       |           |               |
| 5195     | ♀   | 184              | 0.4            |       | 137       |               |
|          |     | 159              |                |       |           | 10/24/84      |
| 5196     | ♀   | 169              | 0.4            |       | 116       |               |
|          |     | 160              |                |       |           | 10/27/84      |
| 5197     | ♀   | 175              | 0.4            |       | 226       |               |
|          |     | 190              |                |       |           |               |
| 5198     | ♀   | 169              | 0.4            | 10:15 | 122       |               |
|          |     | 146              |                |       |           | 10/25/84      |

Necropsy Findings (N = None) 10/23/84

| See Individual  | Animal # | Day | Day | Day |
|-----------------|----------|-----|-----|-----|
| Necropsy Sheets |          | -1  | 0   | 1   |
|                 | 5189     | 287 | 283 | 316 |
|                 | 5190     | 270 | 259 | 305 |
|                 | 5191     | 262 | 250 | 271 |
|                 | 5192     | 268 | 244 | 266 |
|                 | 5193     | 278 | 266 | 300 |
|                 | 5194     | 187 | 173 | 192 |
|                 | 5195     | 201 | 193 | 209 |
|                 | 5196     | 187 | 179 | 122 |
| COMMENTS:       | 5197     | 200 | 188 | 201 |
|                 | 5198     | 185 | 170 | —   |

10/23/84 10/24/84 10/25/84

| TOXIC SIGNS *                           | HOURS |   | DAYS |   |    |   |   |   |   |   |   |   |   |    |    |    |
|---|-------|---|------|---|----|---|---|---|---|---|---|---|---|----|----|----|
|   | 0     | 1 | 2    | 4 | 24 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
| No signs                                | 1     | 1 | 1    | 1 | 1  | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1  | 1  | 1  |
| Increased activity                      |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Decreased activity                      |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Convulsions, clonic                     |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| tonic                                   |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Axonia                                  |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Straub tail                             |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Paralysis                               |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Diarrhea                                |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Salivation                              |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Lacration                               |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Ptosis                                  |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Poor grooming                           |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Exophthalmos                            |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Chromodacryorrhea                       |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Pilo-erection                           |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Muscle tone: increased                  |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| decreased                               |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Abnormal gait                           |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Abnormal stance                         |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Dyspnea                                 |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Cyanosis                                |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Body drop                               |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Tremors                                 |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Loss of righting reflex                 |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Prostration                             |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Others                                  |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Brown discoloration<br>mucosa-mat. inc. |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| slow breathing                          |       |   |      |   |    |   |   |   |   |   |   |   |   |    |    |    |
| Mortality (AM)                          | 0     | 0 | 0    | 0 | 0  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0  | 0  | 0  |
| Mortality (PM)                          | +     | 0 | 0    | 0 | 0  | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0  | 0  | 0  |

\*0 hours refer to immediate post-dose observation.

\*Top half of each block refers to males; bottom half to females.

Technical performance: Mammal Pathology

Study Director: Dr. J. L. Smith, Jr., Ph.D.



PHARMAKON RESEARCH INTERNATIONAL, INC.  
WAVERLY, PENNSYLVANIA 18471

PHONE  
(717) 688-2411

Individual Necropsy Sheet

| Study No. PH402-EH0081 | Species: Rat    | Sex: ♂                          | Weight: 364 | Date: 11/1/84 |     |              |   |     |       |
|------------------------|-----------------|---------------------------------|-------------|---------------|-----|--------------|---|-----|-------|
| Animal #: 5189         | Ear Tag #: 5189 | Reason*: 1 (2) 3 4 (circle one) |             |               |     |              |   |     |       |
| Compound: Saytex 115   | Dose: 5000mg/kg | Study Director: J. Mallay       |             |               |     |              |   |     |       |
| Tissue                 | E               | Wt.                             | Tissue      | E             | Wt. | Tissue       | E | Wt. | Other |
| Brain                  | ✓               |                                 | Heart       | ✓             |     | Cecum        | ✓ |     |       |
| Sp. Cord               | ✓               |                                 | Liver       | ✓             |     | Colon        | ✓ |     |       |
| Pituitary              | ✓               |                                 | Cholecyst   |               |     | Mesen.l.node | ✓ |     |       |
| Eyes                   | ✓               |                                 | Kidneys     | ✓             |     | Testes       | ✓ |     |       |
| Sal. glands            | ✓               |                                 | Spleen      | ✓             |     | Epididymis   | ✓ |     |       |
| Submn.l.node           | ✓               |                                 | Pancreas    | ✓             |     | Prostate     | ✓ |     |       |
| Thyroid                | ✓               |                                 | Urocyst     | ✓             |     | Seminal ves. | ✓ |     |       |
| Parathyroid            | ✓               |                                 | Adrenals    | ✓             |     | Ovary        |   |     |       |
| Thymus                 | ✓               |                                 | Stomach     | ✓             |     | Uterus       |   |     |       |
| Esophagus              | ✓               |                                 | Duodenum    | ✓             |     | Sternebrae   |   |     |       |
| Trachea                | ✓               |                                 | Jejunum     | ✓             |     | Sciatic n.   |   |     |       |
| Lung                   | ✓               |                                 | Ileum       | ✓             |     | Skel. muscle |   |     |       |

E= examine Wt. = weight(gm) \*1 = dead 2 = term sac 3 = sac morib 4 = sac weak

Necropsy Observations (NVL = no visible lesions):

N.V.L.

JM

Prosector: Susan E. Ammondi Pathologist:

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## PHARMAKON RESEARCH INTERNATIONAL, INC.

WAVERLY, PENNSYLVANIA 16471

PHONE  
(717) 586-2411

## Individual Necropsy Sheet

| Study No: PHX02 ET 01084 | Species: Rat    | Sex: ♂   | Weight: 333 | Date: 11/1/84 |     |              |   |     |       |
|--------------------------|-----------------|--|-------------|---------------|-----|--------------|---|-----|-------|
| Animal #: 5190           | Ear Tag #: 5190 | Reason*: 1 <input checked="" type="radio"/> 2 <input type="radio"/> 3 <input type="radio"/> 4 (circle one) |             |               |     |              |   |     |       |
| Compound: Saitex 115     | Dose: 5000mg/kg | Study Director: J. Malloy  |             |               |     |              |   |     |       |
| Tissue                   | E               | Wt.  | Tissue      | E             | Wt. | Tissue       | E | Wt. | Other |
| Brain                    | ✓               |  | Heart       | ✓             |     | Cecum        | ✓ |     |       |
| Sp.Cord                  | ✓               |  | Liver       | ✓             |     | Colon        | ✓ |     |       |
| Pituitary                | ✓               |  | Cholecyst   |               |     | Mesen.l.node | ✓ |     |       |
| Eyes                     | ✓               |  | Kidneys     | ✓             |     | Testes       | ✓ |     |       |
| Sal. glands              | ✓               |  | Spleen      | ✓             |     | Epididymis   | ✓ |     |       |
| Submn.l.node             | ✓               |  | Pancreas    | ✓             |     | Prostate     | ✓ |     |       |
| Thyroid                  | ✓               |  | Urocyst     | ✓             |     | Seminal ves. | ✓ |     |       |
| Parathyroid              | ✓               |  | Adrenals    | ✓             |     | Ovary        |   |     |       |
| Thymus                   | ✓               |  | Stomach     | ✓             |     | Uterus       |   |     |       |
| Esophagus                | ✓               |  | Duodenum    | ✓             |     | Sternebrae   |   |     |       |
| Trachea                  | ✓               |  | Jejunum     | ✓             |     | Sciatic n.   |   |     |       |
| Lung                     | ✓               |  | Ileum       | ✓             |     | Skel. muscle |   |     |       |

E= examine Wt. = weight(gm) \*1 = dead .2 = term sac 3 = sac morib 4 = sac weak

Necropsy Observations (NVL = no visible lesions):

N.V.L.

JPM

Prosector: June E. Almondri Pathologist:

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## PHARMAKON RESEARCH INTERNATIONAL, INC.

WAVERLY, PENNSYLVANIA 18471

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(717) 686-2411

## Individual Necropsy Sheet

| Study No. <i>PHY02ET01084</i> | Species: <i>Rat</i>    | Sex: <i>♂</i>  | Weight: <i>177g</i> | Date: <i>10/24/84</i> |     |              |   |     |       |
|-------------------------------|------------------------|--|---------------------|-----------------------|-----|--------------|---|-----|-------|
| Animal #: <i>5191</i>         | Ear Tag #: <i>5191</i> | Reason*: <input checked="" type="radio"/> 1 2 3 4 (circle one) |                     |                       |     |              |   |     |       |
| Compound: <i>Sautex 115</i>   | Dose: <i>500mg/kg</i>  | Study Director: <i>V. Malley</i>                               |                     |                       |     |              |   |     |       |
| Tissue                        | E                      | Wt.  | Tissue              | E                     | Wt. | Tissue       | E | Wt. | Other |
| Brain                         | /                      |  | Heart               | /                     |     | Cecum        | / |     |       |
| Sp.Cord                       | /                      |  | Liver               | /                     |     | Colon        | / |     |       |
| Pituitary                     | /                      |  | Cholecyst           |                       |     | Mesen.l.node | / |     |       |
| Eyes                          | /                      |  | Kidneys             | /                     |     | Testes       | / |     |       |
| Sal. glands                   | /                      |  | Spleen              | /                     |     | Epididymis   | / |     |       |
| Submn.l.node                  | /                      |  | Pancreas            | /                     |     | Prostate     | / |     |       |
| Thyroid                       | /                      |  | Urocyst             | /                     |     | Seminal ves. | / |     |       |
| Parathyroid                   | /                      |  | Adrenals            | /                     |     | Ovary        |   |     |       |
| Thymus                        | /                      |  | Stomach             | /                     |     | Uterus       |   |     |       |
| Esophagus                     | /                      |  | Duodenum            | /                     |     | Sternebrae   |   |     |       |
| Trachea                       | /                      |  | Jejunum             | /                     |     | Sciatic n.   |   |     |       |
| Lung                          | /                      |  | Ileum               | /                     |     | Skel. muscle |   |     |       |

E= examine Wt. = weight(gm) \*1 = dead 2 = term sac 3 = sac morib 4 = sac weak

Necropsy Observations (NVL = no visible lesions):

Several dark patchy areas on all lung lobes  
 intestines fluid filled yellow-black.

Prosector:

*John E. Ammonk*

Pathologist:

*Notebook #1019 Page 112*

## PHARMAKON RESEARCH INTERNATIONAL, INC.

WAVERLY, PENNSYLVANIA 18471

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## Individual Necropsy Sheet

|                        |                 |                               |             |               |
|------------------------|-----------------|-------------------------------|-------------|---------------|
| Study No: PH402ET01054 | Species: Rat    | Sex: ♂                        | Weight: 311 | Date: 11/1/84 |
| Animal #: 5192         | Ear Tag #: 5192 | Reason*: 1 2 3 4 (circle one) |             |               |

|                      |                  |                            |           |   |     |              |   |     |       |
|----------------------|------------------|----------------------------|-----------|---|-----|--------------|---|-----|-------|
| Compound: Saytex 115 | Dose: 5000 mg/kg | Study Director: D. Mallory |           |   |     |              |   |     |       |
| Tissue               | E                | Wt.                        | Tissue    | E | Wt. | Tissue       | E | Wt. | Other |
| Brain                | ✓                |                            | Heart     | ✓ |     | Cecum        | ✓ |     |       |
| Sp.Cord              | ✓                |                            | Liver     | ✓ |     | Colon        | ✓ |     |       |
| Pituitary            | ✓                |                            | Cholecyst |   |     | Mesen.l.node | ✓ |     |       |
| Eyes                 | ✓                |                            | Kidneys   | ✓ |     | Testes       | ✓ |     |       |
| Sal. glands          | ✓                |                            | Spleen    | ✓ |     | Epididymis   | ✓ |     |       |
| Submn.l.node         | ✓                |                            | Pancreas  | ✓ |     | Prostate     | ✓ |     |       |
| Thyroid              | ✓                |                            | Urocyst   | ✓ |     | Seminal ves. |   |     |       |
| Parathyroid          | ✓                |                            | Adrenals  | ✓ |     | Ovary        |   |     |       |
| Thymus               | ✓                |                            | Stomach   | ✓ |     | Uterus       |   |     |       |
| Esophagus            | ✓                |                            | Duodenum  | ✓ |     | Sternebrae   |   |     |       |
| Trachea              | ✓                |                            | Jejunum   | ✓ |     | Sciatic n.   |   |     |       |
| Lung                 | ✓                |                            | Ileum     | ✓ |     | Skel. muscle |   |     |       |

E= examine Wt. = weight(gm) \*1 = dead 2 = term sac 3 = sac morib 4 = sac weak

"necropsy Observations (NVL = no visible lesions):

N.V.L.

J.M.

Prosector: Susan Amondi Pathologist:

Notebook #1019 page 113

## PHARMAKON RESEARCH INTERNATIONAL, INC.

WAVERLY, PENNSYLVANIA 18471

PHONE  
(717) 686-2411

## Individual Necropsy Sheet

| Study No. PH407-ETO/108 | Species: Rat    | Sex: ♂   | Weight: 187g. | Date: 10/27/84 |     |              |   |     |       |
|-------------------------|-----------------|--|---------------|----------------|-----|--------------|---|-----|-------|
| Animal #: 5193          | Ear Tag #: 5193 | Reason*: <input checked="" type="radio"/> 1 2 3 4 (circle one) |               |                |     |              |   |     |       |
| Compound: Daytek 115    | Dose: 5000mg/kg | Study Director: J. Mallory                                     |               |                |     |              |   |     |       |
| Tissue                  | E               | Wt.  | Tissue        | E              | Wt. | Tissue       | E | Wt. | Other |
| Brain                   | ✓               |  | Heart         | ✓              |     | Cecum        | ✓ |     |       |
| Sp.Cord                 | ✓               |  | Liver         | ✓              |     | Colon        | ✓ |     |       |
| Pituitary               | ✓               |  | Cholecyst     |                |     | Mesen.l.node | ✓ |     |       |
| Eyes                    | ✓               |  | Kidneys       | ✓              |     | Testes       | ✓ |     |       |
| Sal. glands             | ✓               |  | Spleen        | ✓              |     | Epididymis   | ✓ |     |       |
| Submn.l.node            | ✓               |  | Pancreas      | ✓              |     | Prostate     | ✓ |     |       |
| Thyroid                 | ✓               |  | Urocyst       | ✓              |     | Seminal ves. | ✓ |     |       |
| Parathyroid             | ✓               |  | Adrenals      | ✓              |     | Ovary        |   |     |       |
| Thymus                  | ✓               |  | Stomach       | ✓              |     | Uterus       |   |     |       |
| Esophagus               | ✓               |  | Duodenum      | ✓              |     | Sternebrae   |   |     |       |
| Trachea                 | ✓               |  | Jejunum       | ✓              |     | Sciatic n.   |   |     |       |
| Lung                    | ✓               |  | Ileum         | ✓              |     | Skel. muscle |   |     |       |

E= examine Wt. = weight(gm) \*1 = dead .2 = term sac 3 = sac morib 4 = sac weak

Necropsy Observations (NVL = no visible lesions):

adrenals dark red  
 intestines fluid-filled dark green  
 stomach multiple lesions (black) within

JHM

Prosector: Diane E. Almondri Pathologist:

Notebook #1019 page 114

## PHARMAKON RESEARCH INTERNATIONAL, INC.

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## Individual Necropsy Sheet

| study No: PH402-E10/81 | Species: Rat    | Sex: ♀                          | Weight: 215g. Date: 11/1/84 |   |     |              |   |     |       |
|------------------------|-----------------|---------------------------------|-----------------------------|---|-----|--------------|---|-----|-------|
| Animal #: 5194         | Ear Tag #: 5194 | Reason*: 1 (2) 3 4 (circle one) |                             |   |     |              |   |     |       |
| Compound: Saytex 115   | Dose: 5000mg/kg | Study Director: D. Malby        |                             |   |     |              |   |     |       |
| Tissue                 | E               | Wt.                             | Tissue                      | E | Wt. | Tissue       | E | Wt. | Other |
| Brain                  | ✓               |                                 | Heart                       | ✓ |     | Cecum        | ✓ |     |       |
| Sp.Cord                | ✓               |                                 | Liver                       | ✓ |     | Colon        | ✓ |     |       |
| Pituitary              | ✓               |                                 | Cholecyst                   |   |     | Mesen.1.node | ✓ |     |       |
| Eyes                   | ✓               |                                 | Kidneys                     | ✓ |     | Testes       |   |     |       |
| Sal. glands            | ✓               |                                 | Spleen                      | ✓ |     | Epididymis   |   |     |       |
| Submn.1.node           | ✓               |                                 | Pancreas                    | ✓ |     | Prostate     |   |     |       |
| Thyroid                | ✓               |                                 | Urocyst                     | ✓ |     | Seminal ves. |   |     |       |
| Parathyroid            | ✓               |                                 | Adrenals                    | ✓ |     | Ovary        | ✓ |     |       |
| Thymus                 | ✓               |                                 | Stomach                     | ✓ |     | Uterus       | ✓ |     |       |
| Esophagus              | ✓               |                                 | Duodenum                    | ✓ |     | Sternebrae   |   |     |       |
| Trachea                | ✓               |                                 | Jejunum                     | ✓ |     | Sciatic n.   |   |     |       |
| Lung                   | ✓               |                                 | Ileum                       | ✓ |     | Skel. muscle |   |     |       |

E= examine Wt. = weight(gm) \*1 = dead 2 = term sac 3 = sac morib 4 = sac weak

Necropsy Observations (NVL = no visible lesions):

N.V.L.

JFM

Prosector: Shann E. Ammondi Pathologist:

Notebook #1019 Page 115

## PHARMAKON RESEARCH INTERNATIONAL, INC.

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PHONE  
(717) 586-2411

## Individual Necropsy Sheet

| Study No. A402-ET-01084 | Species: Rat    | Sex: ♀                        | Weight: 137g. | Date: 10/24/84 |     |              |   |     |       |
|-------------------------|-----------------|-------------------------------|---------------|----------------|-----|--------------|---|-----|-------|
| Animal #: 5195          | Ear Tag #: 5195 | Reason*: ① 2 3 4 (circle one) |               |                |     |              |   |     |       |
| Compound: Saytex 115    | Dose: 5000mg/kg | Study Director: J. Mallay     |               |                |     |              |   |     |       |
| Tissue                  | E               | Wt.                           | Tissue        | E              | Wt. | Tissue       | E | Wt. | Other |
| Brain                   | ✓               |                               | Heart         | ✓              |     | Cecum        | ✓ |     |       |
| Sp.Cord                 | ✓               |                               | Liver         | ✓              |     | Colon        | ✓ |     |       |
| Pituitary               | ✓               |                               | Cholecyst     |                |     | Mesen.l.node | ✓ |     |       |
| Eyes                    | ✓               |                               | Kidneys       | ✓              |     | Testes       |   |     |       |
| Sal. glands             | ✓               |                               | Spleen        | ✓              |     | Epididymis   |   |     |       |
| Submn.l.node            | ✓               |                               | Pancreas      | ✓              |     | Prostate     |   |     |       |
| Thyroid                 | ✓               |                               | Urocyst       | ✓              |     | Seminal ves. |   |     |       |
| Parathyroid             | ✓               |                               | Adrenals      | ✓              |     | Ovary        | ✓ |     |       |
| Thymus                  | ✓               |                               | Stomach       | ✓              |     | Uterus       | ✓ |     |       |
| Esophagus               | ✓               |                               | Duodenum      | ✓              |     | Sternebrae   |   |     |       |
| Trachea                 | ✓               |                               | Jejunum       | ✓              |     | Sciatic n.   |   |     |       |
| Lung                    | ✓               |                               | Ileum         | ✓              |     | Skel. muscle |   |     |       |

E= examine Wt. = weight(gm) \*1 = dead 2 = term sac 3 = sac morib 4 = sac weak

## Necropsy Observations (NVL = no visible lesions):

*Liver: pale  
intestines fluid-filled yellow-green*

Prosector: *A. M. A. Ammondi* Pathologist: *J. Mallay*

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## PHARMAKON RESEARCH INTERNATIONAL, INC.

WAVERLY, PENNSYLVANIA 18471

PHONE  
(717) 588-2411

## Individual Necropsy Sheet

| Study No. PH402 ET-01084 | Species: Rat    | Sex: ♀                        | Weight: 116g. | Date: 10/07/84 |     |              |   |     |       |
|--------------------------|-----------------|-------------------------------|---------------|----------------|-----|--------------|---|-----|-------|
| Animal #: 5196           | Ear Tag #: 5196 | Reason*: ① 2 3 4 (circle one) |               |                |     |              |   |     |       |
| Compound: Sautex 115     | Dose: 500mg/kg. | Study Director: J. Mallory    |               |                |     |              |   |     |       |
| Tissue                   | E               | Wt.                           | Tissue        | E              | Wt. | Tissue       | E | Wt. | Other |
| Brain                    | ✓               |                               | Heart         | ✓              |     | Cecum        | ✓ |     |       |
| Sp. Cord                 | ✓               |                               | Liver         | ✓              |     | Colon        | ✓ |     |       |
| Pituitary                | ✓               |                               | Cholecyst     |                |     | Mesen.l.node | ✓ |     |       |
| Eyes                     | ✓               |                               | Kidneys       | ✓              |     | Testes       |   |     |       |
| Sal. glands              | ✓               |                               | Spleen        | ✓              |     | Epididymis   |   |     |       |
| Submn.l.node             | ✓               |                               | Pancreas      | ✓              |     | Prostate     |   |     |       |
| Thyroid                  | ✓               |                               | Urocyst       | ✓              |     | Seminal ves. |   |     |       |
| Parathyroid              | ✓               |                               | Adrenals      | ✓              |     | Ovary        | ✓ |     |       |
| Thymus                   | ✓               |                               | Stomach       | ✓              |     | Uterus       | ✓ |     |       |
| Esophagus                | ✓               |                               | Duodenum      | ✓              |     | Sternebrae   |   |     |       |
| Trachea                  | ✓               |                               | Jejunum       | ✓              |     | Sciatic n.   |   |     |       |
| Lung                     | ✓               |                               | Ileum         | ✓              |     | Skel. muscle |   |     |       |

E= examine Wt. = weight(gm) \*1 = dead 2 = term sac 3 = sac morib 4 = sac weak

NVL = no visible lesions)

intestines fluid filled red-green  
 stomach: multiple lesions (black) within.

JM

Prosector: June E. Almondri Pathologist:

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## PHARMAKON RESEARCH INTERNATIONAL, INC.

WAVERLY, PENNSYLVANIA 18471

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(717) 586-2411

## Individual Necropsy Sheet

|                      |              |        |              |               |
|----------------------|--------------|--------|--------------|---------------|
| Study No: PHOT-01084 | Species: Rat | Sex: ♀ | Weight: 226g | Date: 11/1/84 |
|----------------------|--------------|--------|--------------|---------------|

|                |                 |                                 |
|----------------|-----------------|---------------------------------|
| Animal #: 5197 | Ear Tag #: 5197 | Reason*: 1 (2) 3 4 (circle one) |
|----------------|-----------------|---------------------------------|

|                      |                |                           |
|----------------------|----------------|---------------------------|
| Compound: Saytex 115 | Dose: 500mg/kg | Study Director: J. Muller |
|----------------------|----------------|---------------------------|

| Tissue       | E | Wt. | Tissue    | E | Wt. | Tissue       | E | Wt. | Other |
|--------------|---|-----|-----------|---|-----|--------------|---|-----|-------|
| Brain        | / |     | Heart     | / |     | Cecum        | / |     |       |
| Sp.Cord      | / |     | Liver     | / |     | Colon        | / |     |       |
| Pituitary    | / |     | Cholecyst |   |     | Mesen.l.node | / |     |       |
| Eyes         | / |     | Kidneys   | / |     | Testes       | / |     |       |
| Sal. glands  | / |     | Spleen    | / |     | Epididymis   |   |     |       |
| Submn.l.node | / |     | Pancreas  | / |     | Prostate     |   |     |       |
| Thyroid      | / |     | Urocyst   | / |     | Seminal ves. |   |     |       |
| Parathyroid  | / |     | Adrenals  | / |     | Ovary        | / |     |       |
| Thymus       | / |     | Stomach   | / |     | Uterus       | / |     |       |
| Esophagus    | / |     | Duodenum  | / |     | Sternebrae   |   |     |       |
| Trachea      | / |     | Jejunum   | / |     | Sciatic n.   |   |     |       |
| Lung         | / |     | Ileum     | / |     | Skel. muscle |   |     |       |

E= examine Wt. = weight(gm) \*1 = dead 2 = term sac 3 = sac morib 4 = sac weak

Necropsy Observations (NVL = no visible lesions):

N.V.L.

-J.M.

Prosector: Diane E. Almondi Pathologist:

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## PHARMAKON RESEARCH INTERNATIONAL, INC.

WAVERLY, PENNSYLVANIA 18471

PHONE  
(717) 586-2411

## Individual Necropsy Sheet

| Study No: PH402-EF-010-84 | Species: Rat    |     | Sex: ♀                        | Weight: 122g. | Date: 10/25/84 |              |   |     |       |
|---------------------------|-----------------|-----|-------------------------------|---------------|----------------|--------------|---|-----|-------|
| Animal #: 5198            | Ear Tag #: 5198 |     | Reason*: ① 2 3 4 (circle one) |               |                |              |   |     |       |
| Compound: Saytex 115      | Dose: 5000mg/kg |     | Study Director: J. Mallory    |               |                |              |   |     |       |
| Tissue                    | E               | Wt. | Tissue                        | E             | Wt.            | Tissue       | E | Wt. | Other |
| Brain                     | ✓               |     | Heart                         | ✓             |                | Cecum        | ✓ |     |       |
| Sp.Cord                   | ✓               |     | Liver                         | ✓             |                | Colon        | ✓ |     |       |
| Pituitary                 | ✓               |     | Cholecyst                     |               |                | Mesen.l.node | ✓ |     |       |
| Eyes                      | ✓               |     | Kidneys                       | ✓             |                | Testes       |   |     |       |
| Sal. glands               | ✓               |     | Spleen                        | ✓             |                | Epididymis   |   |     |       |
| Submn.l.node              | ✓               |     | Pancreas                      | ✓             |                | Prostate     |   |     |       |
| Thyroid                   | ✓               |     | Urocyst                       | ✓             |                | Seminal ves. |   |     |       |
| Parathyroid               | ✓               |     | Adrenals                      | ✓             |                | Ovary        | ✓ |     |       |
| Thymus                    | ✓               |     | Stomach                       | ✓             |                | Uterus       |   |     |       |
| Esophagus                 | ✓               |     | Duodenum                      | ✓             |                | Sternebrae   |   |     |       |
| Trachea                   | ✓               |     | Jejunum                       | ✓             |                | Sciatic n.   |   |     |       |
| Lung                      | ✓               |     | Ileum                         | ✓             |                | Skel. muscle |   |     |       |

E= examine Wt. = weight(gm) \*1 = dead 2 = term sac 3 = sac morib 4 = sac weak

Necropsy Observations (NVL = no visible lesions):

intestines fluid-filled (yellow-green).

*JHM*

Prosector: Susan E. Almondri

Pathologist:

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